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Biology Behind The Regeneration: A Short Review

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ABSTRACT:

The conception and excogitation of stem cells in the field of life sciences, is an emerging popularity in the field of research, the main objective of this article is to review the literature and science behind the success of stem cell research concerning its application in various medical fields, especially in dentistry. The adult dental ectomesenchymal stem cells are gaining popularity they seem to be promising results for future regenerative therapy. Stem cells have been isolated from human dentition; they can be differentiated into many dental components, such as dental pulp tissue, dentin, periodontal ligament and cementum, except enamel. New reports and outcome of various researches say that stem cells possess the ability to regenerate nerves tissues and other body tissues. Hence with these properties and abilities of dental stem cells, we can imagine future of dentistry with the legal belief and confidence with which the generation in future can gather an idea to overcome all life-threatening disorders and malformations.

KEYWORDS: Regeneration, Regrowth, Stem cells

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INTRODUCTION:

Stem cells are generally known as clonogenic cells that are capable of repairing and regenerating the diseased tissue, these cells posses the ability of both self renewal and multi-lineage differentiation. Post-natally these stem cells can be obtained and isolated from various body tissues like, bone marrow, neural tissue, skin, retina, and dental epithelium[1,8]. The damage that are caused to human body either by burn injury, accidents, traumas and diseases that can lead to injuries of soft tissue, peripheral nerve tissue, and various other organs of the body, which often results in disability of the organ and neuralgic pain. Hence to overcome disabilites of the organs and nerve tissues, the discovery of stem cells was done. The healing and regeneration of the diseased nerve tissue after trauma or injury, is strongly dependent on the contribution of schwann cells to regenerate the tissue or organ, the regenerative capacity of nerves is strongly enhanced in the presence of schwann cells [2]. These cells not only reconstitute myelin tissue, but enhance the fast recovery of neural action potential propagation and also provide trophic support and physical guidance for regeneration of axonal tissue. Dental pulp being the most important soft tissue component within a tooth, contains stem cells, known as dental pulp stem cells. The finest and abundant stem cells are found in a pulp of deciduous teeth also known as milk teeth. The stem cells obtained from the deciduous teeth are of 'mesenchymal' type of cells i.e. this kind of cells possess the ability to generate a wide variety of cell types like osteoblasts, adipocytes and chondrocytes. Osteoblasts are cells that have the ability to generate bones. Chondrocytes are cells that have the ability to generate cartilage, which can play an important role in the treatment of arthritis and joint injuries. Adipocytes are cells that have the ability to compose adipose tissue, specialized in storing energy as fat. In essence, dental stem cells can generate solid structures of the body such as bone, new dental tissue, cartilage and muscle, since they will be equipped with the means to rectify and regenerate parts of their own bodies. Atari m et al, established a protocol for isolating and identifying the subpopulations of pluripotent- like stem cells from the dental pulp (dppsc) these cells are ssea4+, oct3/4+, nanog+, sox2+, lin28+, cd13+, cd105+, cd34-, cd45-, cd90+, cd29+, cd73+, stro1+ and cd146-, and they show genetic stability in vitro based on genomic analysis with a newly described technique [3, 5]. Adult stem cells, such as mesenchymal stem cells, these cells are promising candidates to treat peripheral nerve injuries. Mesenchymal stem cells have been shown to secrete and produce neurotrophic factors, that is required for inducing axonal outgrowth, and they can differentiate into schwann-like cells or neurons. The stem cells can be isolated from extracted tooth especially from the impacted third molar and deciduous tooth are harvested from ectodermal derived cells that possesses the properties of

mesenchymal cells. The advantage of using extracted impacted and deciduous tooth is that to obtain stem cell and no invasive procedures are required these cells can be directly harvested from wisdom tooth. Furthermore, their stem cell properties are retained after cryopreservation, providing the opportunity to establish a stem cell bank regeneration of the disrupted human nervous system from disease or trauma is a challenge for stem cell-based therapeutic paradigms. Thus, in model organisms, both endogenous and exogenous neural stem cells have been investigated for their capacity to regenerate a damaged nervous system [2, 6].

DISCUSSION:

The most commonly used cells in regenerative therapy via stem cells are the mesenchymal stem cells, these cells are non hematopoietic, multipotent cells in nature that possess the ability to proliferate rapidly and can be differentiated into a range of types of cells that comprise various tissues. These cells were first discovered 48 years ago, by dr friedenstein and his team; they identified and demonstrated specific properties in these cells such as: their morphology is like fibroblastic cell; they possess the ability to grow on tissue-culture surfaces, and are osteogenic dominance in nature. These cells are multipotent in nature and can be differentiated to neuroblasts, osteoblasts, cartilage, and muscle, endothelial and adipose cells. The availability and the source of mesenchymal stem cells are commonly found in dental pulp tissue, periodontal ligaments, skeletal muscle, adipose tissue, joint fluid, cord blood, amniotic fluid, and umbilical cord. The easiest source of obtaining stem cells for use in dentistry is done by extracting these cells and from dental tissue itself. The main advantage of using dental stem cells over other tissues is its easy availability. There are numerous sources of stem cells availability from tooth alone. According to their parts and position in the tooth morphology they can be differentiated and grouped as: dental pulp stem cells, human exfoliated deciduous teeth, extracted wisdom tooth, periodontal ligament cells, and dental follicle stem cells [Fig1], stem cells from the dental apical papilla [1, 2, 4]. The use of exogenous sources of stem cells with neural potential has been suggested as a plausible approach to stem cell therapy. Although the stem cells obtained from bone marrow and embryonic cells have been proved to be having greater advantages and are ideal components to treat most of the disease of nerve tissue therapy, and for the neuronal therapy the cells obtained from cranial crest cells adult stem cell populations derived from cranial neural crest cells may possess a greater propensity for neuronal differentiation and repair. The stem cell niches, these are obtained from various parts of adult tissues including skin, hair follicles, intestine, bone marrow, brain, and pancreas.[2] the stem cells that are

harvested from dental pulp are often highly vascularized in nature. The maintenance of these stem cell populations are controlled by the local environment according to the requirements guidelines of the host tissue. Both the connective tissues of dental pulp tissue and bone marrow cells posses populations of stromal stem cells that are capable of high proliferative potentials to regenerate and repair respective tissue and organs with remarkable ability to differentiate, including the surrounding micro structure and mineralized structures of dentine and bone. In the postnatal organism, bone marrow stroma exists as a loosely woven, highly vascularized tissue that supports and regulates hematopoiesis. Adult bone marrow are strong components they retains the ability of continuously renewal of hematopoietic parenchymal tissue and is also responsible for remodeling the adjoining bone surfaces, the bone marrow still remain strong even when many tissues have lost their ability to regenerate. Stem cells are non specialized type of cells that constantly divide, and have the capacity of self-renewal, and are possess the ability of regenerating the diseased tissue and the complex organs. The stem cells are classified based on their natal conditions they can be embryonic, prenatal and/or postnatal. Embryonic stem cells are found in early stages of development of embryo mainly seen in the inner cell mass of the blastocyst. These cells are getting more importance and are obtaining publicity due to their ability to regenerate and possess a potential of self-renewal factor to generate new tissues and organs that makes the application of these in various regenerative therapies by gaining an attractive cellular source for cell-based regenerative treatment modalities[8] however, the use and application of these stem cells is in human regenerating capacity is still in controversial status. Due to its complications, legalization and ethical clearance issues have significantly reduced the feasibility of use of stem cells in the medical and dental field. Postnatal cells are multipotent in nature. However, these stem cells posses limited ability to differentiate into other cell types than the embryonic stem cells. But the advantage of postnatal stem cells is such that they can be used as a source of cells for autologous type of transplants, with greater ability to reduce and minimize the risk factor of rejection of cells due to immune response. The postnatal stem cells can be obtained from the individuals at any stage in lifetime. Studies from the early 1990s demonstrated that bone morphogenic proteins induce the generation of dentin in animal models. However, the ability to induce the formation of dentin is not only limited to bone morphogenic proteins.

But dentin matrix protein has also been shown to nucleate and form the apatite crystals and also to induce dentin formation. The regenerative capability of these stem cells hold a better application in replacing the tissues based on the patients individual needs and are very useful in replacing the tissues in medical and dental conditions.[4]

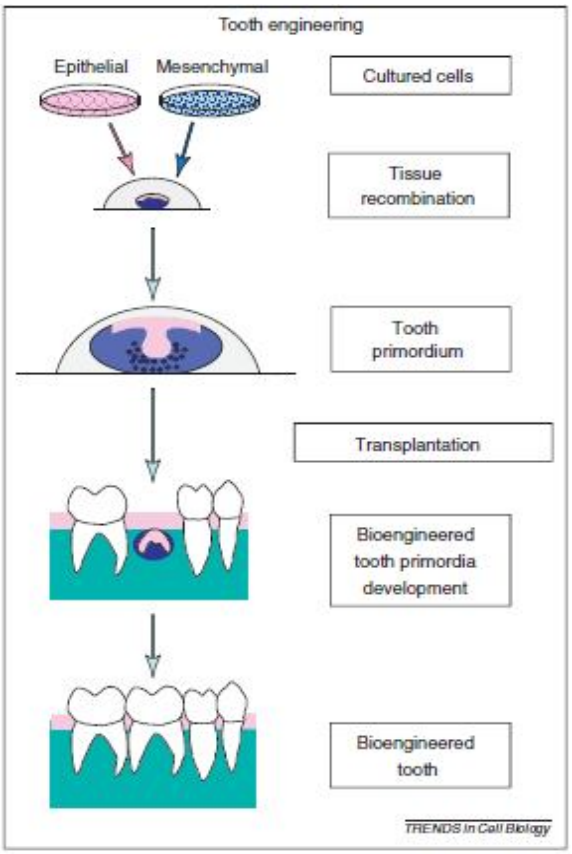

Fig 1, Tooth regeneration by cell re-aggregation [2]

The use of these stem cells in regenerating and replacing the diseased tissue possess a high risk factor, due to its complicating factor and success rate. Hence extreme care should be taken while handling and dealing with stem cells. Hence, its outcome should be thoroughly analyzed in regenerative treatment modalities[11]. The manipulation and processing, storage and transplantation of stem cells to the patients carries the major risk factors. The cells should be free of contamination with the foreign bodies and also pathogenic bacteria's during the process of transplantation. Indeed, patients should be informed about the risk factors and the informed written consent should be obtained from patient and his care taker, and the whole procedure about the treatment and its possible outcomes should be explained. However the future and the outcome of regenerative therapy through stem cells will depend on the understanding of the reaction of the body and the overall microbiology of the cells used to repair and regenerate tissues with in-depth knowledge of the potential risks factors and benefits. The use of stem cells in dentistry is a most complex and multidisciplinary approach.

TABLE 1 - **Schematic representation of various types of stem cells obtained from dental tissues** [9]

Stem Cells	**Target Tissue/Target Cells**	**Literature**
DPSC	ODOOBLASTS	Batouli Et Al 2003, Braut et al, 2004, Iohara et al. 2004, Nakashima et al. 2004, Zhang el at .2005 Huang Et Al, 2006 , Zhang et al, 2008b, Nakashima el at. 2002, He F. et al 2009, Yu J. et al, 2008, Sumita et al. 2009.
	DENTINE & PULP TISSUE	
	OSTEOBLAST	Granthos et al. 2002, Yu J et al 2006, El Backly et all. 2008, He H et al.
	CHONDROCYTES	Granthos et al. 2000, Granthos et al . 2002, Braut et al.2003, Mina & Braut 2004, Laino et al. 2005, Graziano Et Al 2008, et al. 2008, Takeda et al. 2008, Yu J et al. 2008, Koyama et al.2009
	ADIPOCYTES	Kerkis et al.2006, Cheng et al. 2008, Koyama et al, 2009
	ENDOTHELOCYTES	Pierdomenico Et Al. 2005, Jo et al 2007, Liu H. S. et al 2007, Cheng et al .2008, Koyama et al 2009
	NEURONS	D' Aquino et al. 2007 Granthos et al. 2002, Kerkis et al. 2006, D' Aquino et al. 2007, Liu H. S.Et Al 2007, He H et al. 2008.
	MUSCULATURE	Kerkis et al.2006, Zhang et al.2008a.
SHEDS	ODONTOBLATS	MURA et al.2003, CORDIERO et al.2008,SEO et al.2008, SINGHATANADGIT et al.2009, XU N. et al 2009, Zhang et al.2009, Koyama et al 2009
	OSTEOBLASTS	
	NEURONS	
	ADIPOCYTES	MURA et al.2003,
	ENDOTHELOCYTES	MURA et al.2003, XU N. et al 2009, Koyama et al 2009 CORDIERO et al,. 2008
PDLSCS	ODONTOBLATSTS	TRUBIANI et al. 2007
	PERIODONTAL LIGAMENT	SEO et al.2004, SONOMAYA et al,2009. LIU Y. etal 2008, YANG Z. etal 2009
	OSTEOBLAST	GAY et al, 2007. FUJII et al. 2008, CHANG et al. 2009 SINGHATANADGIT et al. 2006.
	CEMENTOBLASTS	SEO et al ,2004. MA et al. 2008, CHANG et al. 2009 . YANG Z. etal 2009.
	CHONDROCYTES	GAY et al.2007
	ADIPOCYTES	SEO et al. 2004, GAY et al, FUJII et al. 2008
DFSCS	PDL PROGENITOR CELLS	YOKOI et al, 2007

	OSTEOBLASTS CEMENTOBLASTS NEUROBLASTS	MORSCZEK et al. 2005, MORSCZEK et al 2006, MORSCZEK et al, 2009a. MORSCZEK et al, 2005, MORSCZEK, 2006, KEMOUN et al. 2007, Wu J.et al. 2008b VOLLNER et al. 2009, MORSCZEK et al. 2009b.
SCAPS	ODONTOBLASTS OSTEOBLASTS	KIKUCHI et al. 2004, SONOYAMA etal. 2006IKEDA et al. 2006, TETE et al. 2008, PARK et al. 2009.

The application and use of stem cells will basically depend on the understanding between the clinicians and research personals; the multidisciplinary team approach is mandatory to regenerate dental and craniofacial tissues. Loss or absence of the tooth due to trauma or caries or any of the pathological conditions is a most common circumstance. The replacement and/or restoring of the missing tooth either with the implant prosthesis, fixed partial denture and removable partial denture prosthesis is very common but the most important aspect of replacing tooth hampers the life of adjacent tooth to prevent such conditions using stem cells has better option in field of dental and aesthetic dentistry.

Many scientists worldwide are working and more focused on tooth tissue engineering, as a potential treatment modality, existing prosthetic methods are most commonly used treatment modalities for replacing tooth, but. Tooth engineering and application of stem cells is a promising new therapeutic approach that seeks to replace/regenerate the missing tooth with tissue engineering/stem cells to restore the damaged/ lost tooth tissue. The dental pulp tissue and periodontal tissues where more of mesenchymal stem cells are found in abundant are more commonly used as a therapeutic modality[2, 9]. The cells are differentiated based on their location or part of tooth [TABLE 1][9]. The stem cells extracted from periodontal ligament and also from dental pulp tissue are commonly applicable in regenerating tissues through tissue engineering, still more research has to be done to conclude the success and the risk factor and also to check for the outcome and its availability other then tooth, in general the other sources of stem cells should be discovered.[1, 12] research should also be done to use other cells, other then mesenchymal cells, the usage of epithelial cells has to be done as it possess a very important source for regenerating enamel tissue. Nevertheless, the outcome and the results and success of the existing stem cells studies are more encouraging and strongly supporting its application in the medical and dental

field, and success of stem cells can set up a new era in replacing the missing tissues for the patients who are suffering due to loss of tooth and tooth analogue [10].

CONCLUSION:

Based on the analysis of the existing literature, clinical experience and research works going on, the concept of use of stem cells in repairing and regenerating the damaged tissue in dental and craniofacial field is in high demand. It is likely that such approaches will involve the use of stem cell-based therapies combined with biomimetic approaches. Although the regenerative properties of the stem cells, have lead the scientists to conclude that these cells are responsible for the restoration/regeneration of lost/missing tissue, yet still more research has to be continued to overcome the possible risk factors of using stem cells and also to establish the advanced techniques to obtain stem cells from various sources and to expand the application of stem cells in medical and dental field.

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